suspected persistent asthma. Preschool-aged children (12–53 months old) with recurrent wheezing received daily budesonide 500 mcg or beclomethasone 400 mcg twice daily compared with intermittent ICS use for 1 to 2 weeks during exacerbations.

No statistically significant difference was noted between the interventions for exacerbations requiring steroids at 12 to 52 weeks follow-up (2 RCTs, n=498; 28% vs 25%; relative risk [RR] 1.1; 95% CI, 0.85–1.4). In school-aged children (5–15 years old) with symptomatic mild persistent asthma not currently using ICS, daily use of inhaled budesonide ranging from 100 to 500 mcg beclomethasone per day was compared with its use only during exacerbations. No difference was noted between the interventions for exacerbations requiring steroids at 12 to 44 weeks follow-up (2 RCTs, n=329; 22% vs 22%; RR 1.3; 95% CI, 0.84–1.9).¹

Individual pediatric studies showed no statistically significant difference in emergency department visits or hospitalizations, but did favor daily ICS over intermittent ICS in mean number of symptomatic days (2 trials, n=214; mean difference [MD] –7% days; 95% CI, –14% to –1%) and proportion of asthma control days (3 trials, n=330, MD –9%; 95% CI, –14% to –4%). A statistically significant difference was noted in change of height from baseline favoring intermittent ICS use (4 trials, n=532; MD 0.41 cm; 95% CI, 0.13–0.69). Limitations of the studies include underpowered sample sizes and short follow-up of a year or less.¹

In children with mild persistent asthma, the National Heart, Lung, and Blood Institute’s National Asthma Education and Prevention Program evidenced-based guidelines from 2007 recommends initiating a low-dose daily ICS as first-line treatment based on strong evidence from RCTs, and does not consider intermittent dosing as an option.²

**In pregnant women undergoing induction with misoprostol, is vaginal or oral dosing better?**

**EVIDENCE-BASED ANSWER**

Vaginal and oral misoprostol are comparable in pregnant women undergoing third trimester induction of labor as far as the outcomes of vaginal delivery not achieved in 24 hours, caesarean section, serious neonatal morbidity or perinatal death, and serious maternal morbidity or death. Vaginal misoprostol is associated with higher rates of postpartum hemorrhage and lower 5-minute Apgar scores than oral (SOR: B, based on systematic review of quality RCTs). The World Health Organization (WHO) recommends either low-dose vaginal or oral misoprostol for induction of labor at term for women who have not had a previous cesarean section; while the American Congress of Obstetricians and Gynecologists (ACOG) recommends oral over vaginal misoprostol (SOR: C, evidence-based guidelines).

A 2014 Cochrane review of 37 RCTs (N=6,417) assessed the efficacy of oral misoprostol for labor induction in women who required third trimester induction with a viable fetus compared with vaginal misoprostol.¹ Primary outcomes included vaginal delivery not achieved in 24 hours, uterine hyperstimulation with fetal heart rate changes, caesarean section, serious neonatal morbidity or perinatal death, and serious maternal morbidity or death.

At lower doses of oral misoprostol (25 mcg), the incidence of uterine hyperstimulation was similar to vaginal misoprostol (25–100 mcg) (risk ratio [RR] 0.30; 95% CI, 0.07–1.2), but higher oral doses of misoprostol (200 mcg) were associated with increased risk of hyperstimulation than vaginal misoprostol (RR 1.6; 95% CI, 1.1–2.4). No significant differences were seen in the rates of caesarean section (RR 0.93; 95% CI, 0.81–1.1), serious neonatal morbidity/death (RR 0.80; 95% CI, 0.60–1.3), serious maternal morbidity/death (RR 2.0; 95% CI, 0.19–20.9), or rates of vaginal delivery not achieved in 24 hours (RR 1.1; 95% CI, 0.86–1.4). Oral misoprostol was associated with a reduction in low Apgar score at 5 minutes (RR 0.60; 95% CI, 0.44–0.82), lower rates of postpartum hemorrhage.

Is progesterone an effective treatment for preventing miscarriage in unexplained recurrent pregnancy loss?

**EVIDENCE-BASED ANSWER**

Progesterone reduces the odds of miscarriage for women who have experienced 3 or more consecutive pregnancy losses (odds ratio [OR] 0.39) compared with placebo, but does not alter outcomes in women with 1 or 2 prior unexplained miscarriages (SOR: B, meta-analysis of small RCTs). An older report from the Royal College of Obstetricians and Gynaecologists (RCOG) found insufficient evidence to assess the effect of progesterone and did not recommend any empiric treatment of recurrent pregnancy loss (SOR: C, expert opinion).

A 2013 systematic review and meta-analysis of 14 RCTs (N=1,458) studied both the efficacy of progesterone to prevent miscarriage in the general population and any adverse events associated with its use.¹ Trials included women with no history of miscarriage and women with recurrent miscarriages. In trials that exclusively enrolled women with a history of pregnancy loss, the losses were all unexplained. Women were randomized to progesterone (oral, intramuscular, intravaginal, implant) or placebo; however, in some trials the controls received no treatment. A multitude of progesterone formulations and schedules were used. The primary outcome was miscarriage. The secondary outcomes for mothers were severity of morning sickness, thrombotic events, depression, admission to special care unit, and subsequent fertility. Secondary outcomes for babies were preterm birth, stillbirth, neonatal death, birth weight less than 2,500 g, genital abnormalities, teratogenic effects, and admission to special care unit.

Progesterone did not reduce the odds of miscarriage in the general population (14 trials, n=1,458; OR 0.99; 95% CI, 0.78–1.2) or in women with 2 or more pregnancy losses (10 trials, n=450; OR 0.68; 95% CI, 0.43–1.1). Progesterone did reduce the odds of miscarriage in women with 3 or more consecutive pregnancy losses (4 trials, n=225; OR 0.39; 95% CI, 0.21–0.72). No significant differences were noted in the secondary outcomes between the 2 groups. The funnel plot showed no evidence of publication bias, and the overall

---

**EVIDENCE-BASED PRACTICE LEARNING OBJECTIVES**

1. To become knowledgeable about evidence-based solutions to commonly encountered clinical problems.

2. To understand how groundbreaking research is changing the practice of family medicine.

3. To become conversant with balanced appraisals of drugs that are marketed to physicians and consumers.